## REMARKS

The Amendment, filed in response to the Office Action mailed July 21, 2009, is believed to fully address all and every issue raised in the Action. Favorable reconsideration and allowance of the application are respectfully requested.

**Disposition of Claims**

Claims 1-10 are all the claims pending in the application. Claims 6 and 7 are amended to remove improper multiple dependency. No claims are canceled or added. No new matter is introduced.

**Priority Document**

While acknowledgment is made of applicant's claim for foreign priority based on an application filed in the Republic of Korea on 26 March 2004, Applicants note that, as the Examiner indicates, a certified copy of the 10-2004-0020800 application was not filed.

Accordingly, a certified copy of this priority document is submitted under a separate cover.

**Information Disclosure Statement**

With regard to the PTO/SB/08 filed on September 25, 2006, the Examiner has not considered KR 2003-64986 and KR 2004-9983 listed therein, as copies of them have not been made available.

A copy of these documents were filed via EFS on October 27, 2009. Consideration of the references and returning an initialed copy of the SB08 Form are respectfully requested.

**Claim Objections**

In the Office Action, claims 6-7 are objected to under 37 CFR 1.75(c) as being in improper form.

In response, claims 6 and 7 are amended to remove improper multiple dependency. Consideration of claims 6 and 7 are respectfully requested.

**Response to Claim Rejections - 35 USC § 103**

1. Summary of the Rejection Grounds

In the Action, claims 1-5 and 8-10 are rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Lee et al. (J. of Invest. Dermat., listed by Applicant in Information Disclosure Statement) and Ahn et al. (KR 10-2003-0075492, abstract, cited in PTO-892).

Lee et al. is relied on as teaching the skin protective properties of ginsenoside Fl, wherein ginsenoside F1 is suggested to protects cells against UVB induced apoptosis by maintaining constant levels of Brn-3a and inhibiting Bcl-2 down regulation. The Examiner refers to page 607 of Lee reference to argue that Lee teaches UVB causes said Bcl-2 down regulation via down regulation of said Brn-3a transcription factor in human HaCaT keratinocytes.

Ahn is cited as teaching a cosmetic composition comprising epigallocatechin-3-gallate (EGCG) that inhibits aging of the skin.

2. Claimed Subject Matter Shows Unexpectedly Superior Synergic Effects

Applicants respectfully traverse the rejection.

In Example 1 in the specification of the instant application, Applicants showed that the combination of 2 μM ginsenoside F1 + 10 μM EGCG showed about 2-fold inhibitory effects on UV-caused apoptotic cell death compared to untreated control groups, while 2 μM ginsenoside

F1 alone or 10 μM EGCG alone did not show any anti-apoptotic effects compared to the untreated control groups. Examples 2-5 further show the synergic effects of the combined use of ginsenoside F1 and EGCG.

In order to further show the synergic effects were not predicted or obvious, Applicant performed further experiments on the combinations of ginsenoside F1 + Quercetin, EGCG + Quercetin, and Quercetin alone (in various concentrations). Quercetin was reported to show anti-apopototic effects at 25 μM concentration, but not at 5 μM concentration. See, Kim & Jang, Ann. N. Y. Acad. Sci., 1171: 305-313(2009) ("Kim reference (2009)"), of which a copy is submitted under a separate cover. In this regard, Applicants note that no IDS is required for submission and consideration of Kim reference, as it is submitted in support of Applicant's arguments which are made in response to the Examiner's rejection. The following experiments show that combinations of Quercetin (at 5 μM) + ginsenoside F1 (at 2 μM) or Quercetin (at 5 μM) + EGCG (at 10 μM) do not show anti-apoptotic effects, whereas the combination of ginsenoside F1 (2 μM) + EGCG (10 μM) showed anti-apoptotic effects (Example 1 in the specification).

Experiment Method

Anti-apoptotic effects of combined treatment with ginsenoside F1, Quercetin and EGCG in HaCaT cells were tested as follows:

[Step 1] Cell line and cell culture

Cell lines used in this experiment and the culture thereof were the same as used in Step 1 of Example 1.

[Step 2] Inhibition of UV-induced apoptosis in HaCaT cells by a combined treatment with ginsenoside F1 + Quercetin, or EGCG + Quercetin

Quercetin was reported as anti-apoptotic agent. E.g., Kim and Jang, "Protective mechanism of quercetin and rutin using glutathione metabolism on HO-induced oxidative stress in HepG2 cells," Ann. N. Y. Acad. Sci. 2009 Aug., 1171:530-7. A copy of Kim reference is submitted under a separate letter.

Cell lines cultured in Step 1 were treated with trypsin to give a single-cell suspension and seeded into a 6-well microplate at $2x10^5$ cells per well, then cultured for 24 hours. Subsequently, the culture medium was refreshed with serum-free DMEM and cells were cultured for another 24 hours. The microplate was then treated with 5 μM Quercetin; 25 μM Quercetin; a combination of 2 μM ginsenoside F1 + 5 μM Quercetin; 5 μM Quercetin + 10 μM EGCG. For reference, ginsenoside F1 was dissolved in 100% ethanol at a 1/1000-fold concentration to the medium and EGCG (Sigma) and Quercetin (Sigma) were dissolved in dimethyl sulfoxide (DMSO) at a 1/1000-fold concentration to the medium, and then added at the required amount to the culture mediums.

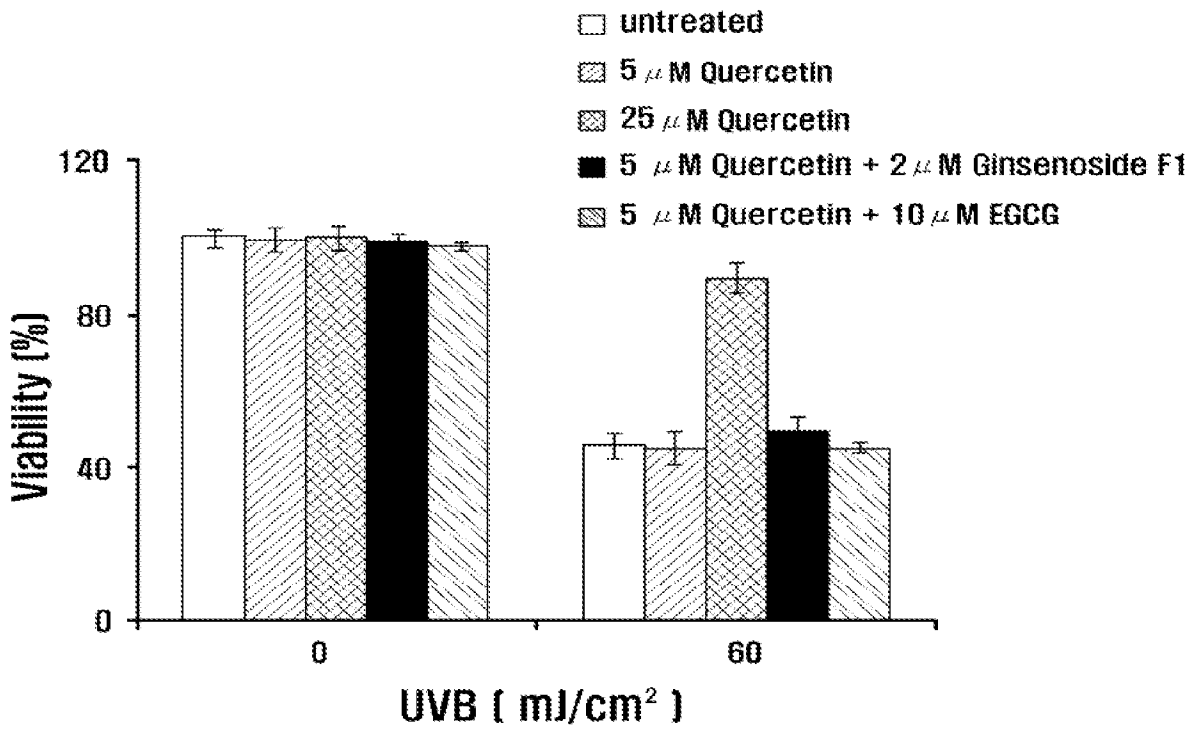
After 24-hour treatment of each test sample, each microplate was washed with phosphate buffered saline (PBS) and exposed to 60 $mJ/cm^2$ of UVB in the presence of PBS. PBS was then removed and the culture medium was refreshed with a medium containing each compound at the corresponding concentration. As a control, untreated cells were cultured in the same way.

24 hours after UV irradiation, to the microplates treated with each compound or untreated was added 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, Sigma) solution, and then the cells were cultured at 37°C for 4 hours. DMSO was added and dissolved completely. The optical density (OD) of formazan formed at 540 nm was measured using an ELISA reader (Thermo Max, Molecular Devices Co.). Cell viability in each test group was

evaluated as a relative value, considering OD of untreated control cells as 100%. The results are shown in the Figure below.

As shown in the Figure, the treatment with 5 μM Quercetin alone showed no difference in UV-caused apoptotic cell population compared with untreated control cells, although treatment of 25 μM Quercetin inhibited UV-caused apoptotic cell death, as reported in a previous study (e.g., Kim reference (2009)). However, **combined treatments with 2 μM ginsenoside F1 + 5 μM Quercetin or 5 μM Quercetin + 10 μM EGCG did not inhibit UV-caused apoptotic cell death**. That is, **the combinations of ginsenoside F1 or EGCG with other known anti-apoptotic agent (Quercetin) do not show any synergic effects.**

Figure



Conclusion

The results of the above experiments and the results presented in the specification of the instant application clearly show that the synergic effects of the combined use of ginsenoside F1 and EGCG at much lower concentrations than the effective concentrations of respective individual agents on inhibiting UV-caused apoptotic cell deaths are not predictable or obvious.

Accordingly, it is believed that the rejection is not sustainable and withdrawal is respectfully requested.

**Response to Provisional Double Patenting Rejections**

In the Office Action, claims 1-5 and 8-10 of the instant application are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the following copending applications:

(1) Claims 7-10 of copending Application No. 12/135,663 (Your Ref.: PUS-051228, Sughrue REF.: Q108671) (effective US filing date: December 27, 2003) directed to an agent containing ginsenoside F1 which is useful to protect cell against UVB-induced apoptosis) in view of Ahn et al. (KR 10-2003-0075492, abstract, cited in PTO-892);

(2) Claim 6 of copending Application No. 10/586,973 (Your Ref.: PUS-060126; Sughrue Ref.: Q96112) (effective US filing date: June 1, 2004) directed to a method of inhibiting gelatinase comprising applying a composition containing ginsenoside F1 and compound K) in view of Ahn et al. (KR 10-2003-0075492, abstract, cited in PTO-892);

(3) Claims 1-2 of copending Application No. 12/064,887 (effective US filing date: September 8, 2006) directed to an anti-aging composition containing catechins (e.g., EGCG) and

a flavonol in an amount of 0.0001-10 wt%, in view of Lee et al. (J. of Invest. Dermat., cited by Applicant in Information Disclosure Statement),.

(4) Claims 15-17 of copending Application No. 11/443271 (effective US filing date: January 3, 2003), directed to a nanoemulsion containing ginsenoside F1 and compound K, in view of Ahn et al. (KR 10-2003-0075492, abstract, cited in PTO-892).

In response, Applicants respectfully request the provisional rejections be hold abeyance until patentable subject matter is identified.

**Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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